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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,658	12/05/2003	Istvan Szelenyi	034082-001	8943

29858 7590 12/15/2006

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EXAMINER

KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No. 10/727,658	Applicant(s) SZELENYI ET AL.	
	Examiner Brian S. Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 August 2006 and 26 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-26 is/are pending in the application.
- 4a) Of the above claim(s) 17-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-16 and 25-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants election with "neuralgia pain" as the elected species is acknowledged.

Claims 17-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

2. By Amendment filed 04/10/06, claims 1-12 were cancelled and claims 13-26 were added.

However, as discussed above, claims 17-24 are withdrawn from further consideration as being drawn to the non-elected invention. Accordingly, claims 13-16 and 25-26 are currently pending for prosecution on the merits.

3. Applicant's arguments with respect to claims 1-12 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 13-14, 16 and 25-26 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for the specific sodium channel inhibitor (e.g., tolperisone, eperisone, eperisone and silperisone), does not reasonably provide enablement for "sodium channel inhibiting or -influencing substance", "an analog thereof" or "its analogs". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The present invention is drawn to a method of treating neuralgia pain comprising administering a combination of flupirtine and "a sodium channel inhibiting or -influencing substance", "an analog thereof" or "its analogs".

The breadth of the claims is very broad due to plethora of compounds having characteristics of "a sodium channel inhibiting or -influencing substance", "analogs thereof" or "its analogs". For examples, the claimed "a sodium channel inhibiting or -influencing substance" encompasses not only inhibitor of sodium channel including various subunits of voltage-gated sodium channel (e.g., $\beta 1$ -4 subunits) and non-voltaged gated sodium channel but also inhibitors or agonists or partial agonist or antagonists of sodium channel including sodium/hydrogen exchangers, sodium-glucose transporters, sodium/myoinositol cotransporter, Na^+/I^- symporter, sodium/potassium/calcium exchanger, $\text{Na}^+/\text{K}^+/\text{Cl}^-$ cotrasporter and etc...

The relative skill of those in the pharmaceutical art and the unpredictability of the pharmaceutical art are very high. One having ordinary skill in the art would have not known that various classes of compounds encompassed by the instant invention would behave similarly

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under the instantly claimed condition. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved”. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

To practice the instant invention to the claimed scope, applicant would have to screen numerous possible compounds characterized as “a sodium channel inhibiting or –influencing substance” considering the structure-activity relationship of the compounds and then test compounds and extrapolate results to the claimed therapeutic utility. In other words, the instant invention necessitates for the skilled artisan to undergo an exhaustive search for the embodiments suitable to practice the claimed invention.

Although the specification describes tolperisone, eperisone, silperisone, riluzole, prpafenone, lidocaine, flecainide and metixen as suitable “a sodium channel inhibiting or –influencing substance”, “an analog thereof” or “its analogs”, there is no teaching in the specification that any other compounds having “agonists or partial agonist of sodium channel including sodium/hydrogen exchangers, sodium-glucose transporters, sodium/myoinositol cotransporter, Na⁺/I⁻ symporter, sodium/potassium/calcium exchanger, Na⁺/K⁺/Cl⁻ cotrasporter” would have similarly as the exemplified compound. In view of limited numbers of working examples, the insufficient amount of guidance present in the specification, the nature of the invention, the state of art, the breadth of the claim and the relative skills of the artisan and the predictability of the pharmaceutical art where many specific differences or different physicochemical properties are existed among unrelated structural compounds would take

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“undue painstaking experimentation” to practice the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 13-16 and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 13 recites the broad recitation “neuralgia pain”, and the claim also recites “neuropathic pain” which is the narrower statement of the range/limitation. Furthermore, claim 16 recites the broad recitation “tolperisone or its analogs”, and the claim also recites “such as eperisone or silperisone” which is the narrower

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statement of the range/limitation (the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d)).

Regarding claims 14 and 16, the claims recite "analogs thereof". It is not clear what "an analogs thereof" refers to. Although "eperisone or silpersone" are shown in the specification as the specific examples, it is considered that the meaning of the claims should be clear from the wording of the claim alone.

For the examination purpose, the term "an analog thereof" or "its analogs" is interpreted as "eperisone and silpersone".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 13, 15 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobisch et al. (US 5162346) in view of Cai et al. (US 6281211).

Lobisch teaches the use of flupirtine for the treatment of neuralgia (or neuropathic pain), wherein said compound is administered in various dosage forms including oral or parenteral forms (column 2, line 67; column 3, lines 9-18; column 6, lines 42-43; and claim 2).

Cai is being supplied as reference to demonstrate the routine knowledge in using Na⁺ channel blocker such as riluzole, lidocaine, propagenone and semicarbazone derivatives for the treatment neuropathic pain (see particularly "Related Background Art" in column 1, lines 18-56 and "Summary of Actions"; abstract).

The teaching of Lobisch differs from the claimed invention in the combination use of flupirtine and sodium channel blocker such as lidocaine, propagenone and riluzole for the treatment of neuralgia or neuropathic pain. To incorporate such teaching into the teaching of Lobisch, would have been obvious in view of Cai who teaches the use of sodium channel blocker such as riluzol, lidocaine and propagenone for the treatment of neuralgia or neuropathic pain.

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Above references in combination make clear that flupirtine and sodium channel blockers such as lidocaine, propageneone and riluzole have been individually used for the treatment of neuralgia or neuropathic pain. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. *See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).*

With respect to the determination of various dosage forms (e.g., orally, rectally, intravenously, transdermally, subcutaneously or intracutaneously) and the current administration regimen of two drugs (e.g., simultaneously, separately or consecutively), such determination of appropriate dosage forms and administration regiment for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of drug delivery information provided in the prior art references.

7. Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobisch et al. (US 5162346) in view of Cai et al. (US 6281211), and further in view of the applicant's admitted prior art of record (page 3, lines 11-23).

The modified teaching of Lobisch (Lobisch in combination with Cai) includes all that is recited in the claims 15 and 16 except the use of "tolperisone, eprisone and silperisone".

The admitted prior art of record teaches tolperisone as sodium channel blocker similar to lidocaine.

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One having ordinary skill in the art would have expected that tolperisone would behave similar as to the known sodium channel blocker such as lidocaine and provide therapeutic utility in the treatment of neuralgia or neuropathic pain through sodium channel blocking mechanism. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Conclusion

8. No Claim is allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system,

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see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Patent Examiner
AU 1614

BRIAN-YONG S. KWON
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Brian', with a long horizontal line extending to the right.